

# MEMORANDUM

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BASIC  
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE  
PUBLIC HEALTH SERVICE  
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION

TO : Director, CDC

DATE: November 21, 1972

FROM : Chief, VD Branch

SUBJECT: Requests for Information Pertaining to the "Tuskegee Study" by the Ad Hoc Advisory Panel

1. The Tuskegee Syphilis Study Ad Hoc Advisory Panel has requested information from the Center for Disease Control pertaining to the following points:
  - A. The results expected from the study;
  - B. The results obtained from the study;
  - C. A review of the knowledge of syphilis as it existed in 1932
2. With regard to Point 1, we have compiled such statements as we could find written in the early 1930's which have some bearing on the results of the study anticipated at that time. With regard to Point 2, we have attempted to list both the actual and the potential scientific contributions of this study, as viewed from our own 1972 perspective. With regard to Point 3, we have been in a quandry: The knowledge of syphilis in 1932 was extensive, and was sufficient to fill several large medical textbooks devoted solely to syphilis. (An example of one is Stokes, John H., *et. al.*, *Modern Clinical Syphilology*. Philadelphia, Pa.: W. B. Saunders Co., Second Edition, 1934.) Realizing that the Panel could obtain specific questions in whatever depth they might desire, we chose to reproduce a section on syphilis which appeared in a well known and widely used text of the day: Cecil, Russell L. (ed.): *A Textbook of Medicine*. Philadelphia, Pa.: W. B. Saunders Co., 1931, pp. 423-445. We hope this will be sufficient to provide the Panel with a summary of syphilis knowledge existing in the 30's which meets their general needs.
3. The responses to the 3 points are attached in individual sections.

For/ Ralph B. Hodges, MD  
John D. Millar, M.D.

Attachment

## SECTION I: RESULTS EXPECTED FROM TUSKEGEE STUDY AS OF 1930'S

Letter From Lida J. Usilton, ScD. Member, VD Program, USPHS, 1930-32

In 1929 the idea was conceived of making a serological survey of the Negroes of the rural south for the purpose of demonstrating the prevalence of syphilis in this racial group and to determine whether or not treatment for syphilis might be applied under conditions met with in the various communities....

Another question which was of great importance in the treatment of syphilis in a rural community was the ascertainment of the correct relation which a syphilis control program should have to the general health program in the community. The various demonstrations have shown that the most practicable administration of syphilis control can take place only when it is integrated with a general health program and, if reasonable success is to be hoped for, a well organized county health unit should exist in the community in which it is to be undertaken.

Before the projects were begun, it was hoped that the amenability of syphilis to control by this method would be demonstrated, that the efficacy of the treatment scheme could be shown and that possibly the direct and indirect effects of syphilis in the morbidity and mortality rates in the Negro population might be measured. An evaluation of results obtained from the treatment of syphilis is of necessity an extremely involved and complicated procedure. Considerable expenditure for social work would be required and it is doubtful whether an accurate estimate could be arrived at in less than ten years since the tendency of the disease to become latent and remain quiescent for long periods of time works against a rapid summing up of results. Indeed, at the present stage of our epidemiological knowledge of syphilis, it is not known just how and at what stage the disease is spread. Most observers feel that syphilis is usually transmitted in its early stage either from open lesions on the external genitalia or from secretions of the inner genital tract. During the later course of the marked process open lesions are rarer and when present, seldom present the causative organism. It has been assumed also that secretions from the inner genital tract are also non-infectious during this period, but this assumption has not been proven absolutely, and recent experimental investigations on the morphology of the spirochete suggest that the organism may be present and may be transmitted even in latent and late syphilis. Because of this, some say to treat only early causes. A paucity of funds might justify such a course; but it is obvious that until more thorough knowledge of the epidemiology of this disease is at hand, no program may be regarded as thorough unless it includes plans to extend treatment to everyone who may be infected regardless of the stage of the disease.

A determination of the effectiveness of treatment in preventing the transmission of syphilis is one of the basic problems in the control of this disease. Second in importance to it, is the effect which treatment has in preventing late and crippling manifestations. The administration of adequate treatment in early syphilis is recognized as the most important factor in the prevention both of communicable relapse and of the early complications so detrimental to the health of the individual patient. As the result of surveys made a few years ago in southern rural areas, it was learned that a considerable portion of the infected Negro population remained untreated during the entire course of syphilis. Such individuals seemed to offer an unusual opportunity to study the untreated syphilitic patient from the beginning of the disease to the death of the infected person. An opportunity was also offered to compare the syphilitic process uninfluenced by modern treatment, with the results obtained when treatment has been given.

Annual Report of the Surgeon General of the Public Health Service of the United States 1931-1932:

The demonstrations inaugurated to show the practicability of man's treatment of syphilis in the rural Negro on an extensive scale in six southern states in 1929-1930 have been completed.... In addition to demonstrating the prevalence of syphilis in the Negro in the rural south, these projects indicated the practicability of man's treatment of this population group and furnished valuable information on the needed financial outlay.

Annual Report of the Surgeon General of the Public Health Service of the United States 1932-1933:

A project was started to study the late effects of untreated syphilis in the Negro for comparison with treated groups of syphilitic individuals of this race. A county in a state of the far south, with a large Negro population and with rather inadequate facilities in the outlying districts for the treatment of syphilis, was selected so that the greatest number of cases of untreated syphilis might be uncovered with a minimum of effort and expenditure.

A preliminary check-up indicates that syphilis of the cardiovascular system is extremely common in this racial group and shows that any comprehensive method for the control of heart disease among Negroes must give thorough consideration to the influence of syphilis. Syphilis of the skin and osseous system was also fairly common in the group studied, and involvement of the CNS was not infrequent, but was usually of a muscular type.

The treatment of syphilis under ideal conditions is of the utmost value in the control of this insidious disease; but, unfortunately, owing to various social and economic influences the ideal method of therapy is seldom possible of attainment, and the vast majority of infected

people receive treatment which is generally regarded as inadequate or no treatment at all. It is highly desirable, therefore, to ascertain, if possible, the relative benefits accrued from adequate and from inadequate treatment.

Annual Report of the Surgeon General of the Public Health Service of the United States 1935-1936:

Observations have been continued on a group of 400 male Negroes infected with syphilis and now in the latent or late stages of this disease. Most of these individuals have never received modern treatment for their infection. Comparable observations also have been continued on a group of 200 male Negroes who, as far as it has been possible to determine, are not infected with syphilis..... Plans for the continuation of this study are underway. During the last 12 months, success has been obtained in gaining permission for the performance of autopsies on 11/15 individuals who died. Pathologic observations made after death are absolutely essential for the confirmation of the original clinical and laboratory observations. The present study will not only make available comparative information regarding the course of treated and untreated syphilis, but should also solve the problem of the effect of syphilis on the development of such conditions as hypertension and arteriosclerosis and should make it possible to accumulate comparative mortality rates for a group of untreated syphilitic Negroes and Negroes who are known not to be syphilitic.

## SECTION II:

### Actual and Potential

#### Scientific Contributions of the "Tuskegee Study"

Knowledge already gained or potentially able to be gained from this study may be categorized as contributing to improvements in the following areas:

1. Care of the surviving participants,
2. Care of all persons with latent syphilis,
3. The operation of a national syphilis control program,
4. Understanding of the disease of syphilis
5. Understanding of basic disease producing mechanisms.

An outline of specific contributions of the study is attached. The numbers following each contribution refer to the five categories mentioned above, and are ranked with the most important application first.

The present status of each contribution is also given. The categories used are:

- Already realized without further evaluation being advisable,
- Already partially realized, but potentially expandable by further evaluation;
- Not previously presented but potentially expandable by further evaluation;
- Probably not possible to obtain.

Contributions have been divided into three major groups:

- Questions originally addressed by the study,
- Questions posed during the course of the study,
- Additional questions which could be posed.

#### I. Questions originally addressed by the study

##### A. Determination of the natural history of untreated syphilis

1. Mortality rates of untreated syphilis as compared to control (4,3,2,1)

Status: Already realized without further evaluation being advisable.

2. Mortality rates and characteristics of morbidity in untreated syphilis as compared to control (4,3,2,1)

Status: Already partially realized, but potentially expandable by further evaluation



3. Comparison of the risk of intervention (a variety of interventions that change over time) in latent syphilis and the risk of the natural course of the disease. The study was not designed to make a study of intervention because participants were not randomly assigned to intervention and non-intervention groups. However, information might be gained by:

- a. Re-examination of the morbidity and mortality of the participants as a function of the degree of adequacy of treatment among patients with syphilis of different durations.
- b. Comparison of more recent data on the course of syphilis in the study participants. (2,1,3,4)

Status: Already partially realized, but potentially expandable by further evaluation

- B. Infectiousness of latent syphilis - although this question was raised, at least informally, there is no recorded data of either serological or clinical examinations of sexual partners. This question might be answered by:

1. Determination of serologic and clinical evidence of syphilis in present and past sexual partners of the patients (3,4,2,1).

Status: Not previously presented, but potentially expandable by further evaluation

- C. Genetic factors in the natural history of syphilis. Attempts to isolate the influence of race on the natural history of syphilis would require comparison with a non-black population. Such a population with comparable environmental factors is not available (4,5,2,1).

Status: Probably not possible to obtain

## II. Questions posed during the course of the study

- A. Role of treatment of uncomplicated latent syphilis of duration in the prevention of the complications of syphilis (2,1,4,5,3).

Status: Already partially realized, but potentially expandable by further evaluation

- B. Role of treatment of existing syphilis complications on the course of these complications (2,1,4,5,3).

Status: Already partially realized, but potentially expandable by further evaluation

- C. Correlation of patient processes with the clinical examination (2,1,4)

Status: Already partially realized, but potentially expandable by further evaluation

- D. Specificity and sensitivity of standard and developmental serologic tests for syphilis in a longitudinal study (3,4,2).

Status: Already partially realized, but potentially expandable by further evaluation

- E. Comparison of the environmental factors among patients with syphilis with a control group (3,4,5).

Status: Already realized without further evaluation being advisable

### III. Additional questions which could be posed

#### A. Host-Treponemal relationships

1. Determination of the host factors that lead to specific complications in some of the living patients and not in others

- a. Endocrinology
- b. Genetic
- c. Immunologic

1. Cell-mediated immunology
2. Humoral immunology
3. Phagocytic capacity of white cells
4. Response to toxins
5. Exposure to agents that alter immunologic responsiveness (4,5)

Status: Not previously presented but potentially expandable by further evaluation

B. Persistence of treponemal forms or structures in treated and untreated late latent syphilis

1. Examination of multiple anatomical sites immediately after death and of tissue (level and lymph node biopsies) and body fluids (aqueous humor and CSF) during life from patients among those treated, inadequately treated and control population, by one or more of the following techniques:

- a. Darkfield microscopy
- b. Fluorescent darkfield microscopy
- c. Direct and indirect FA stains
- d. Silver stains
- e. Histopathologic studies
- f. Animal inoculation
- g. Electron microscopy (4,5)

Status: Not previously presented but potentially expandable by further evaluation

2. Relationship of the findings of III.B.1. to sero-reactivity (4,5).

Status: Not previously presented but potentially expandable by further evaluation

C. Immunology of syphilis

1. Covered in 3.A.1.c.
2. Specific resistance to treponematoses. Re-exposure to infectious syphilis could probably neither be documented retrospectively nor be expected in the future in patients of the age of the study participants (4,5).

Status: Probably not possible to obtain

3. Role of re-exposure to infectious syphilis in contributing to the development of the complications in latent syphilis. Probably this is unavailable for the same reason as 2 above. (4,5)

Status: Probably not possible to obtain



D. Diagnostic methods - the serologic re-evaluation has been covered in an earlier section.

1. Improvement of methods to detect treponemes - already covered in the section on persistence of forms (4,5,3).

Status: Not previously presented but potentially expandable by further evaluation

2. Evaluation of diagnostic skin tests in latent syphilis (3,4,5,2).

Status: Not previously presented but potentially expandable by further evaluation

E. Therapy of syphilis

1. Evaluation of modifications of currently recommended therapies to cover the possibility of persistent treponemal forms (possible l-forms) in the prevention of either the complications or their progression

Status: Not previously presented but potentially expandable by further evaluation

2. Determination of the risks of therapy in treated and inadequately treated latent syphilis as they relate to a complete clinical evaluation of the patient prior to therapy (1,2,4)

Status: Not previously presented but potentially expandable by further evaluation

3. Determination of the effectiveness of combined antimicrobial and immunosuppressant therapy in the treatment of late latent syphilis (1,2,4).

Status: Not previously presented but potentially expandable by further evaluation

4. Definition of the pathogenesis of the Jarisch-Herxheimer reaction (4,2,1)

Status: Not previously presented but potentially expandable by further evaluation

F. Clinic investigation

Determination of clinical criteria for diagnosing complications of syphilis. Correlation of these criteria with serologic reactivity and patient findings (2,4,1).

Status: Already partially realized, but potentially expandable by further evaluation